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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,896	11/24/2003	Roberto Celeste Ercole Solari	674525-2007	8692

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EXAMINER	
CARLSON, KAREN C	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 02/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/720,896	SOLARI ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,15,22-24 and 27-36* is/are pending in the application.

4a) Of the above claim(s) *28-31 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,15,22-24,27,32 and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/26/04*. ¢ 2003

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

Applicant's election with traverse of Group 1 as drawn to a conjugate comprising a nuclear membrane translocation protein and Notch intracellular domain in the reply filed on December 14, 2005 is acknowledged. The traversal is on the ground(s) that: Applicants state that the inventions are not independent and distinct but do not provide any explanation as to why the restriction was wrong, that is, why the claimed conjugates do not differ in structure and in function. Applicants urge that prosecution is expensive. This is not a consideration for restriction. Applicants state that it would not be a serious burden on the Office for the Examiner to examine the claims because the conjugates are all interrelated. As noted above, Applicants do not provide any explanation why the claimed conjgates do not differ in structure and in function. Therefore, the restriction is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-14, 16-21, 25, and 26 have been canceled. Claims 28, 29-31, and 33 have been withdrawn from further consideration by the Examiner because these claims are drawn to non-elected inventions. Claims 1, 2, 15, 22-24, 27, 32, and 34-36 as they pertain to peptide conjugates are currently under examination.

Priority: May 25, 2001

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 15, 22-24, 27, 32, and 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is comprises reference to non-elected subject matter. Therefore, the claims do not particularly point out and distinctly claim the subject matter which the applicant regards as his elected invention.

Claim 15 depends from cancelled Claim 14. For examining purposes, Claim 15 has been taken to depend from Claim 1.

Claim 15, it is not clear if the second sequence further comprises all of RAM, PEST, and OPA, or in the alternative, that is, any one of or at least one of RAM, PEST, or OPA?

Claims 22 and 27 recite transport protein which has no antecedent basis in Claim 1 which refers to a translocation protein.

In claim 24, it is not clear if "about 60" is the same as "about 40", for example. Also, Claim 24 does not recite a reference sequence identification number for the fragments specified.

In Claim 27, it is not clear what a variant of HIV tat is, that is, whether tat substituted, truncated, and so on.

In Claim 35, it is not clear what disease or infection is being treated.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35 and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 35 and 36 are drawn to methods of treating or preventing disease by administering a conjugate comprising a nuclear membrane transport protein and Notch intracellular domain. This conjugate acts in the nucleus, and therefore would not be expected to function if administered to a subject because the conjugate would have to enter the subject, then the affected cells membrane, traverse the cell cytoplasm, cross the nuclear membrane, and function in the nucleus.

In *Ex parte Forman* (230 USPQ 546) the Board considered the issue of enablement in molecular biology. The Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation:

1) Quantity of experimentation necessary: It is established that the administration of proteins to act intracellularly requires chemical and pharmacological intervention to produce a polypeptide in a form that can be administered to a subject without degradation before the polypeptide gets to its intended site of action. Also, there is no known transport system at the cell membrane to translocate *nuclear* membrane transport protein and (*nuclear*) Notch intracellular domain, thus a hindrance contributing to the activity of this fusion protein in a subject. Further, a method for preventing a disease is absolute, that is, the disease will not present itself in the subject. This requires further experimentation to determine if, when activity is established for treatment of disease, the fusion construct is sufficient to prevent disease.

2) Amount of direction or guidance presented: There is no guidance provided.

3) Presence or absence of working examples: There are no working examples provided.

4) Nature of the invention; 5) State of the prior art; 6) Relative skill of those in the art: The invention is complex and the prior art does not recognize the administration of nuclear bound proteins in a subject. Those working in this art are highly skilled.

7) Predictability or unpredictability of the art: It is not predictable if a pharmaceutical compositions comprising *nuclear* membrane transport protein and (*nuclear*) Notch intracellular domain can be made to translocated into a cell.

8) Breadth of the claims: The claims encompass methods of treating and methods for preventing disease.

For all of these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen Cochrane Carlson PhD

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KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER